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Original Research Article

Comparative study of tear film evaluation among healthy pregnant women and gestational diabetes: a cross-sectional study

Jayakumar Antony Cruse[1], Samuel Livingstone Kumaran[1]*, Tamilselvan Pachiyappan[2]

[1]Department of Optometry, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
[2]Department of Optometry, Mangala Group of Educational Institutions, Mangalore, Karnataka, India

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***Correspondence:**
Samuel Livingstone Kumaran,
E-mail: sml.livingstone@gmail.com

ABSTRACT

Background: Diabetes mellitus (DM) is one of the risk factors for dry eye. This study aimed to estimate the characteristics of tear film by measuring the tear secretion, tear evaporation rate, conjunctival impression cytology and also ocular surface disease index (OSDI) scoring through a questionnaire for gestational diabetes mellitus (GDM) and healthy pregnant women (HPW).
Methods: Total of 40 subjects which included 20 subjects who were HPW in group-1 and 20 subjects who were GDM in group-2. After examining their ocular status, the subjects were initially administered with OSDI questionnaire followed by dry eye evaluation procedures such as non-invasive tear breakup time (NIBUT), Schirmer's 1 and 2, tear film break up time (TBUT) and conjunctival impression cytology (CIC).
Results: The gathered data was checked for normality. Mean and standard deviation was compiled for each parameter for their respective groups. A statistical comparison with independent t test was performed between the groups which compared OSDI scores, NIBUT, Schirmer's 1 and 2, TBUT and CIC for both HPW and GDM group women. Statistically significant difference ($p<0.01$) was observed with OSDI scores, Schirmer's test 2, TBUT and NIBUT whereas Schirmer's test 1 and CIC were not statistically significant ($p>0.01$). OSDI scores represented mild symptoms for GDM women.
Conclusions: Tear film of GDM women was affected more than HPW suggesting evaporative dry eye. Assessing tear film as a part of routine eye examination for women with GDM is essential to avoid the occurrence of complications due to tear film abnormalities.

Keywords: Gestational diabetes mellitus, Pregnant women, Dry eye, Tear film

INTRODUCTION

DM is a syndrome that is caused by a complete or relative deficit of insulin. This can primarily cause many ocular related complications such as lid inflammation, hordeolosis, ptosis, neovascular glaucoma, cataract, diabetic retinopathy, fluctuated refractive component, oculomotor palsy and dry eye syndrome.[1-3] DM can be classified into different types such as type-1 DM, type-2 DM and GDM based on it's cause.[4] Impaired glucose tolerance in GDM is a growing health problem as it affects 1-14% of all pregnancies.[5] India reports close to 16% of pregnant women with GDM.[6] Prevalence of GDM in certain places of Southern India such are Chennai (17%), Erode (18.8%), Bangalore (12%) and Trivandrum (15%). Indian women have nearly 11.3 times greater chance of developing GDM against white women.[6]

Hyperglycemia in pregnant women can cause substantial defects on the ocular surface as well in the tear flim.[7] Tear film spreads quickly and completely on the pre-ocular surface after a complete blink. Stability of tear film is responsible for clear vision and comfort of the eye. They mainly are secreted from lacrimal gland (main and

accessory lacrimal) and also from meibomian glands and goblet cells.[10] The most important lacrimal glands are the tubular acinar serous glands, which consist primarily of acinars, ducts and myoepithelial cells, while acinar cells accounting for 80% of the total.[16] In addition, about forty Krause and Wolfling glands have been added.[11]

There are various factors affecting the tear film such as (1) ocular: rosacea-blepharitis, eye injuries and LASIK refractive surgery; (2) non ocular: autoimmune diseases, lacrimal gland dysfunction and hormonal changes; (3) ageing.[12] A Previous study has reported ocular changes during pregnancy was due to distribution of lacrimal cell.[19] When the physiology of tear film was affected it led to dry eye. Dry eye occurring during pregnancy may resolve postpartum.[15]

Previous studies in DM have reported clinical signs such as less tear secretion and instability, conjunctival squamous metaplasia, low goblet cell density and less corneal sensitivity.[13,17] Complications such as delayed corneal epithelial healing, oedema, recurrent erosions and dry eye were common but under diagnosed in DM (type 1 and 2).[14] Dry eye being dependent on number of factors like the surface of eye and tears which indicated distress, visual instabilities and tear film variability. It also complements increased tear osmolarity and inflammation of ocular surface.[8] Tear components and kerato-conjunctival epithelium gets affected due to various factors leading to ophthalmic constraint and uncharacteristic visual fuctions.[8]

Most of the literature have been towards dry eye and diabetic subjects rather very few have been prospected on GDM. Lack of information about occurrence of dry eye in GDM can well be a concern. Perinatal screening being essential to appreciate the occurrence of any ocular abnormality, performing tear film evaluation as a routine examination in GDM becomes imperative to understand GDM and dry eye.[15] Regulating tear film evaluation as a standard protocol of test can aid in attaining more information towards dry eye in GDM. Considering all these gaps, our study aimed to compare the tear film characteristic between HPW and GDM.

METHODS

Participants

This comparative cross-sectional study was carried out with approval from the institutional research ethics committee (Ref No: IEC CSP/19/MAY/77/174) and adhere to the tenets of the Declaration of Helsinki. Subjects who were HPW (group-1) and subjects who were GDM (group-2) were recruited from the department of gynaecology, tertiary hospital in Chennai, South India based on the eligibility criteria. The participants were selected by convenience sampling. Sample size was calculated before initiation of the study, using the nMaster software version 2.0 with respect to the results of available literature. The required sample size calculated was estimated as 40 (20 in each group). Women with GDM, healthy pregnant women who were in their 2nd and 3rd trimester (from 24 the week of pregnancy) were included in the study. Known history of dry eye, recurrent eye infection, systemic disease caused dry eye like Sjogren's syndrome and 1st trimester pregnant women were excluded.

Tools

OSDI questionnaire, slit lamp, keratometer, Whatman strip no. 41, proparacaine, fluorescein stain and glass slides were the tools used in the study.

Procedure

Selected subjects were assessed for preliminary eye examination which included visual acuity, objective and subjective refraction, pupillary evaluation, extra ocular motility, cover test and slit lamp examination. After confirming their ocular status, the subjects were administered with OSDI questionnaire followed by dry eye evaluation with procedures like NIBUT, TBUT, Schirmer's I and II and CIC.

OSDI questionnaire

The subjects were asked to fill in OSDI to identify their symptoms related to dry eye.[9] The questions were as follows: eyes that were sensitive to light; eyes that felt gritty; painful or sore eyes; blurred vision; poor vision; reading; driving at night; working with a computer or bank machine computer or bank machine (ATM); watching TV; windy conditions; places or areas with low humidity (very dry); areas that are air conditioned.

Subjects were asked to give their responses on a 0 to 4 scale. 0 meant none of the time and 4 meant all of the time. The ocular surface index was estimated was estimated using a formula. The final score was calculated which ranges from 0 to 100 with scores. 0 to 12 represented normal, 13 to 22 represented mild dry, 23 to 32 represented moderate dry eye, and greater than 33 represented severe dry eye.

NIBUT

This test was performed in a room condition with low air speed and low general illumination. The patient was encouraged to sit comfortably on the device and blink freely while looking into to the target in front of them. The patient was asked to stop blinking until instructed to resume. The time from the last full blink to the first display of the occurrence pattern was noted. The normal value considered for NIBUT was >10 seconds.

Schirmer's test

The test began with placing the Whatman filter paper (no. 41) in the inferior temporal conjunctival sac. When anesthetizing, the lower end of the paper was dried to remove the remaining fluid. The strip was taken after 5 minutes and the length to which the paper is moist is noted in millimeters. In general, readings greater than or equal to 10 mm were considered normal cut-off points for both tests. Abnormal findings strongly indicate a lack of tear in dry eye.

Schirmer's test-I: without anaesthesia

Schirmer's test-II: with anaesthesia

TBUT

This test was performed to estimate the local evaporation of the tear film. A fluorescein strip was moistened and placed in the inferior cul-de-sac. Patients were observed in diffuse illumination with a cobalt blue filter in a slit lamp. The time taken for the first appearance of dark spot was noted. 10 seconds or more was considered normal.

CIC

CIC was a non-invasive technique that gave conjunctival-corneal information, cell morphology, cell-to-cell ratio, and interaction of epithelial cells with other cellular components.[32] One to three cell layers were involved in the removal of the conjunctiva and cornea. This gave details on squamous metaplasia of the conjunctival epithelium. Samples of the conjunctiva were taken on slides and stained using Papanicolaou method. After staining, the slides were observed under an optical microscope at a magnification of 400×. The features observed were graded according to the classification system. Nelson's classification for squamous metaplasia and grade features were grade-0: >500 goblet cells/mm^2 small, round epithelial cells with large nuclei; grade-1 to 2: 100-500 goblet cells/mm^2 and grade-3: 100 goblet cells/mm^2 large, polygonal epithelial cells with small nuclei.[32] Grade 2 or more was described as abnormal.

Statistical analysis

The collected data was analysed with statistical package for the social sciences (SPSS) 16.0 version. The data was checked for normal distribution with Shapiro wilk test and independent t test was used to find out the difference in ocular parameters between HPW and GDM as the data was normally distributed. Mean and SD was estimated for continuous variables.

RESULTS

The current research included 40 participants, out of which twenty subjects were HPW and twenty were GDM. The mean and SD of age in years HPW (28.25±2.95) and GDM (28.60±2.16), gestational weeks: HPW (30.40±3.92) and GDM (31.00±3.92) and HbA1c%: HPW (5.44±0.33) and (8.35±0.90) respectively. This study compared OSDI scores, Schirmer's test 1 and 2, TBUT, NIBUT and CI) for both HPW and GDM group women. Statistically significant difference ($p<0.01$) was observed in OSDI score, Schirmer's test 2, TBUT and NIBUT whereas Schirmer's test 1 and CIC were not statistically significant ($p>0.01$) (Table 1).

When comparing the mean values with the available normative data of dry eye, HPW and GDM group showed normal values in Schirmer's 1 and 2.[9] The OSDI scores indicated ocular surface as normal for HPW (3.7±3.44) and mild dry eye symptoms for GDM (12.4±5.66) women. TBUT, NIBUT and CIC didn't resemble normative values in both the groups. The mean values of TBUT, NIBUT and CIC were much lesser in GDM group suggesting dry eye more in GDM women compared to HPW (Figure 1).

Table 1: Comparison of ocular parameters among HPW and GDM.

Ocular parameters	Groups		P value
	HPW	GDM	
	Mean±SD	Mean±SD	
OSDI (score)	3.7±3.44	12.4±5.66	0.000
Schirmer's 1 OD (mm)	19.6±5.33	17.4±6.03	0.229
Schirmer's 1 OS (mm)	18.85±5.37	16.65±5.76	0.219
Schirmer's 2 OD (mm)	19.6±5.33	12.2±3.91	0.002
Schirmer's 2 OS (mm)	18.85±5.37	12.05±4.20	0.005
TBUT OD (secs)	5.85±1.14	4.05±1.47	0.000
TBUT OS (secs)	6.2±1.06	3.9±1.37	0.000
NIBUT OD (secs)	6.65±1.18	4.85±0.93	0.000
NIBUT OD (secs)	6.6±1.14	4.85±1.04	0.000
CIC cell OU	240±59.65	218.5±68.23	0.295

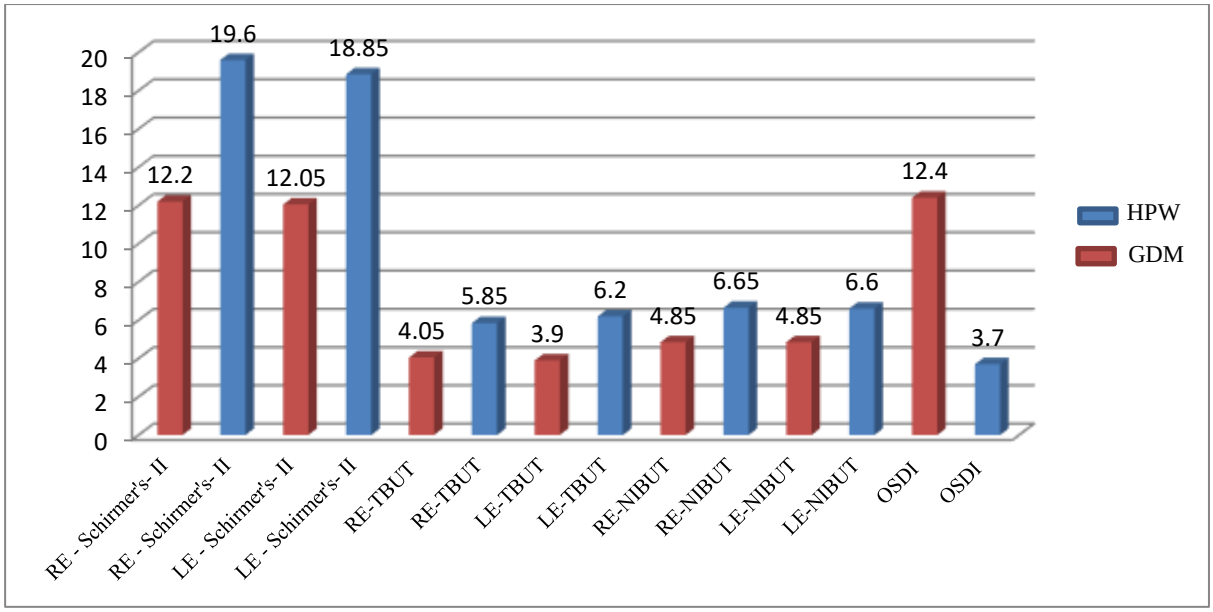

Figure 1: Bar graph representing the mean values of diagnostic tests with significant difference between HPW and GDM.

DISCUSSION

Our study had made the diagnosis of dry eye based on symptom score acquired through OSDI questionnaire and diagnostic tests which included Schirmer's test, TBUT, NIBUT and CIC. To the best of our knowledge only Kan et al had done tear film evaluation among GDM in turkey and this present study was first to evaluate the tear film in pregnant and GDM women in Southern India.[7] Our study reported normal scores with OSDI questionnaire for HPW which meant the HPW group reported no symptoms towards dry eye. On the contrary the TBUT, NIBUT and CIC revealed lesser values (less than the normative values) indicating dry eye and grade 1-2 squamous metaplasia. This might well be a caution to HPW who may lately develop symptoms pertaining to dry eye. Women in GDM group reported OSDI scores which indicated mild dry eye symptoms. As per their symptoms we found values of TBUT, NIBUT and CIC of GDM group were much lesser compared to HPW confirming more dry eye. Lesser values of NIBUT and TBUT in both the groups indicate the pregnant women having evaporative dry eye (EDE).

Previous studies showed that occurrence of dry eye decreased tear secretion and tear stability in pregnant women and also DM as observed in our study.[10,18-21] Though the Schirmer's represented normative values (>10 mm), the mean values were not greater than 20 mm in a 35 mm strip. This meant a possibility of having a gradual reduction in tear secretion which was observed more in GDM than HPW group in our study. The possible reason which could affect the tear secretion was the development and differentiation of Meibomian gland enhanced by testosterone during pregnancy. The reduction in size of the gland due to estrogen promoted acinar cell death leading to decrease tear secretion.[22] This could be one of the reasons as our study showed borderline Schirmer's 2 values for GDM compared to HPW.

It was stated by Alves et al that the dry eye and ocular surface damage due to DM had a chance to increase, when there in an increase of the disease.[17] This meant pregnant women with GDM had higher risk of developing more symptoms in the near future as observed with mild dry eye symptoms during second and third trimester in our study. The prime diagnostic findings of tear instability were TBUT and Schirmer's.[24] The OSDI combined with TBUT and Schirmer's were the best tests to detect the dry eyes.[7] Our study expressed reduced TBUT values, mild range of OSDI scores as obvious signs directing towards EDE in the GDM group. Though Schirmer's 2 value represented was normal, the values were marginal. The values of TBUT in HPW group were less than normative data, but were slightly better than GDM group. This meant HPW being asymptomatic now might well be at risk of developing symptoms later.

The difference found in Schirmer's test 2, between HPW and GDM group indicated pregnant women with diabetes had decreased basal tear secretion and tear stability but within the normative data. Inadequate metabolic control, diabetic neuropathy and retinopathy were some risk factors of reduced basal tear secretion. Schirmer's test 1 measured both basal and reflex tear secretion. Reflex tearing could be one of the contributing factors in not observing any major difference between the groups. Generally, the tear secretory activity was stimulated by the irritation of filter paper.[28] The influential factors of this test were state of patients, location of strips, dryness of remaining fluid in the eyes or not, with open or closed

eye in case of influence from the environment condition or the rate of blinking.[29,30]

LFU (lacrimal function unit) played a major role in tear film formation and maintaining normal physiology of the ocular surface. Tear deficiency or evaporative DES can lead to damage of any component of LFU as observed in our study.[33] Dry eye disease were divided into EDE and aqueous deficient dry eye (ADDE) or a combination of them.[23] TBUT was solely based on thinning of aqueous layer, contact between lipid and mucin layer and neural receptors.[25-27] Other reasons for EDE were eyelid disorders, Meibomian gland dysfunction (MGD), environmental conditions and contact lens use.

Squamous metaplasia was one of the ocular surface changes that was observed in patients with diabetes as observed in our study.[10] The severity of the disease can be estimated by the CIC grading of squamous metaplasia of conjunctival epithelium cell counts which helped in assessing the prognosis of the disease.[31] CIC was a good indicator of mild to moderate dry eye syndrome.[24] The average goblet cell densities less than 500 cells/sqmm indicated an ocular disorder. The mean number of epithelial cell densities observed in this study were reduced in HPW and GDM were the latter had much lesser cell densities.

Kan et al study about the tear film evaluation among GDM between 24 to 28 week of gestational age group resulted no significant effect on the tear functions of the pregnant women due to GDM.[7] This may be because of relatively short exposure time of hyperglycemia on pregnant women, whereas our study involved pregnant women between 24-34 weeks. Inclusion of 3rd trimester pregnant women and diagnostic test like CIC were considered to be the strengths of our study. Though our sample size was limited, future studies with larger sample size and multi-centric approach can aid more information towards this thrust area of research. Lack of supporting literatures on GDM makes it more crucial to assess tear film function among pregnant women especially with diabetes. More research towards GDM and dry eye will provide further evidence towards tear film functions. According to the findings our study we suggest every eye care practitioner to perform a complete dry eye evaluation for pregnant women particularly for women with GDM to rule out any risk factors of dry eye. Implementing OSDI questionnaire can also provide inputs on their level of symptoms.

CONCLUSION

Our study identified tear film of GDM women was affected more than HPW suggesting evaporative dry eye. To avoid the occurrence of complications due to tear film abnormalities, we recommend routine tear film evaluation for a pregnant women in every eye care practice.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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